Retention of Absolute Configuration in Hydrogen Atom Transfer/Cyclisation Cascade

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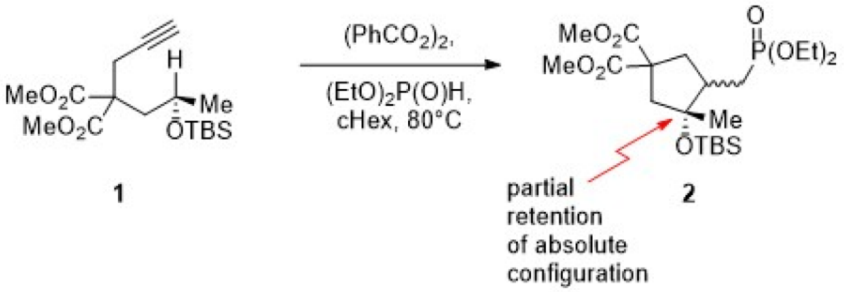
Due to the nature of radicals, few stereoselective reactions are known in which a radical is generated at a chiral center with retention of the absolute configuration. In an early report by Heiba and Dessau, the formation of an optically active lactone was observed although the reaction proceeds through a radical at the chiral center *via* a 1,5-H shift.[1] The level of retention was however unknown. Recently, Curran and coworkers published a related cyclisation process of a-amide radicals involving retention of chirality.[2, 3]

Meanwhile, our group reported a radical cyclisation involving phosphonyl and thiyl radicals to access cyclopentane derivatives.[4] We decided to use this reaction as the starting point to study whether retention of chirality is possible and the factors influencing the stereochemical outcome.

The alkynyl malonate **1** was readily synthesized in a five-step procedure strating from (*S*)-(–)-ethyl lactate. Treatment of **1** with diethylphosphite afforded the cyclic product **2** with partial retention of configuration (Scheme 1)



[1] El-Ahmadi I. Heiba, Ralph M. Dessau, *J. Am. Chem. Soc.*, **1967**, *89*, 2238-2239
[2] Aniruddha Sasmal, Tsuyoshi Taniguchi, Peter Wipf, Dennis P. Curran, *Can. J. Chem.*, **2013**, *91*, 1-5
[3] For a review on memory of chirality see: Hongwu Zhao, Danny C. Hsu, Paul R. Carlier, *Synthesis*, **2005**, 1-16
[4] a) Florent Beaufils, Fabrice Dénès, Phillippe Renaud, *Angew. Chem. Int. Ed.*, **2005**, *44*, 5273-5275
b) Florent Beaufils, Fabrice Dénès, Phillippe Renaud, *Org. Lett.*, **2004**, *6*, 2563-2566